

From the INTERNATIONAL BUREAU

**PCT**

NOTIFICATION OF TRANSMITTAL  
OF COPIES OF TRANSLATION  
OF THE INTERNATIONAL PRELIMINARY REPORT  
ON PATENTABILITY  
(CHAPTER I OR CHAPTER II  
OF THE PATENT COOPERATION TREATY)  
(PCT Rules 44bis.3(c) and 72.2)

To:

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Chiyoda-ku, Tokyo 1000005  
JAPON



Date of mailing (day/month/year) 28 September 2006 (28.09.2006)	
Applicant's or agent's file reference FP0327PCT	<b>IMPORTANT NOTIFICATION</b>
International application No. PCT/JP2005/002389	International filing date (day/month/year) 17 February 2005 (17.02.2005)
Applicant KYORIN PHARMACEUTICAL CO., LTD. et al	

## 1. Transmittal of the translation to the applicant.



The International Bureau transmits herewith a copy of the English translation of the international preliminary report on patentability (Chapter I).



The International Bureau transmits herewith a copy of the English translation of the international preliminary report on patentability (Chapter II).

## 2. Transmittal of the copy of the translation to the designated or elected Offices.

The International Bureau notifies the applicant that copies of that translation have been transmitted to the following designated or elected Offices requiring such translation:

None

The following designated or elected Offices, having waived the requirement for such a transmittal at this time, will receive copies of that translation from the International Bureau only upon their request:

AE, AG, AL, AM, AP, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EA, EC, EE, EG, EP, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OA, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

## 3. Reminder regarding translation into (one of) the official language(s) of the elected Office(s).

The applicant is reminded that, where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary report on patentability (Chapter II).

It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned within the applicable time limit (Rule 74.1). See Volume II of the PCT Applicant's Guide for further details.

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# PATENT COOPERATION TREATY

# PCT

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

Applicant's or agent's file reference FP0327PCT	<b>FOR FURTHER ACTION</b>	See item 4 below
International application No. PCT/JP2005/002389	International filing date ( <i>day/month/year</i> ) 17 February 2005 (17.02.2005)	Priority date ( <i>day/month/year</i> ) 18 February 2004 (18.02.2004)
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237		
Applicant KYORIN PHARMACEUTICAL CO., LTD.		

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 *bis*.1(a).

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

- |                                     |              |   |
|-------------------------------------|--------------|---|
| <input checked="" type="checkbox"/> | Box No. I    | Basis of the report   |
| <input type="checkbox"/>            | Box No. II   | Priority  |
| <input type="checkbox"/>            | Box No. III  | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability  |
| <input type="checkbox"/>            | Box No. IV   | Lack of unity of invention  |
| <input checked="" type="checkbox"/> | Box No. V    | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| <input type="checkbox"/>            | Box No. VI   | Certain documents cited   |
| <input type="checkbox"/>            | Box No. VII  | Certain defects in the international application  |
| <input type="checkbox"/>            | Box No. VIII | Certain observations on the international application   |

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44bis .2).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland  Facsimile No. +41 22 338 82 70	Date of issuance of this report 19 September 2006 (19.09.2006)  Authorized officer  <div style="text-align: center; font-weight: bold; font-size: 1.2em;">Masashi Honda</div>  e-mail: pt08@wipo.int
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# PATENT COOPERATION TREATY

TRANSLATION

From the  
INTERNATIONAL SEARCHING AUTHORITY

PCT

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

To:

Date of mailing  
(day/month/year)

Applicant's or agent's file reference

**FP0327PCT**

**FOR FURTHER ACTION**

See paragraph 2 below

International application No.

**PCT/JP2005/002389**

International filing date (day/month/year)

**17.02.2005**

Priority date (day/month/year)

**18.02.2004**

International Patent Classification (IPC) or both national classification and IPC

Applicant

**KYORIN PHARMACEUTICAL CO., LTD.**

1. This opinion contains indications relating to the following items:

- |                                     |              |  |
|-------------------------------------|--------------|--|
| <input checked="" type="checkbox"/> | Box No. I    | Basis of the opinion   |
| <input type="checkbox"/>            | Box No. II   | Priority   |
| <input type="checkbox"/>            | Box No. III  | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability   |
| <input type="checkbox"/>            | Box No. IV   | Lack of unity of invention   |
| <input checked="" type="checkbox"/> | Box No. V    | Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| <input type="checkbox"/>            | Box No. VI   | Certain documents cited  |
| <input type="checkbox"/>            | Box No. VII  | Certain defects in the international application   |
| <input type="checkbox"/>            | Box No. VIII | Certain observations on the international application  |

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/JP

Authorized officer

Facsimile No.

Telephone No.

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/JP2005/002389

Box No. I

Basis of this opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.  
☐ This opinion has been established on the basis of a translation from the original language into the following language \_\_\_\_\_, which is the language of a translation furnished for the purposes of international search (under Rule 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
  - a. type of material  
☐ a sequence listing  
☐ table(s) related to the sequence listing
  - b. format of material  
☐ in written format  
☐ in computer readable form
  - c. time of filing/furnishing  
☐ contained in the international application as filed.  
☐ filed together with the international application in computer readable form.  
☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/JP2005/002389

**Box No. V** Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

**1. Statement**

Novelty (N)	Claims	<u>1-8</u>	YES
	Claims	_____	NO
Inventive step (IS)	Claims	_____	YES
	Claims	<u>1-8</u>	NO
Industrial applicability (IA)	Claims	<u>1-8</u>	YES
	Claims	_____	NO

**2. Citations and explanations:**

Document 1: US 2002-193390 A1 (Novartis A.-G.), 19 December 2002  
 Document 2: JP 2003-520849 A (Novo Nordisk A/S), 08 July 2003  
 Document 3: JP 2002-356472 A (Tanabe Seiyaku Co., Ltd.), 13 December 2002  
 Document 4: JP 2004-503531 A (Novartis AG.), 05 February 2004  
 Document 5: JP 2004-002368 A (Tanabe Seiyaku Co., Ltd.), 08 January 2004  
 Document 6: JP 2004-002367 A (Tanabe Seiyaku Co., Ltd.), 08 January 2004  
 Document 7: WO 2004/009544 A1 (Yamanouchi Pharmaceutical Co. Ltd.), 29 January 2004  
 Document 8: WO 2003/106456 A2 (Sanofi-Synthelabo), 24 December 2003  
 & WO 2003/106456 A3

[1] The inventions of claims 1-8 do not appear to involve an inventive step based on documents 1, 2, 3-8 cited in the ISR.

Document 1 (page 14, Par. No. 0187) discloses 1-[[4-(pentylbicyclo[2.2.2]oct-1-yl)amino]acetyl]-2-cyano-(S)-pyrrolidine as a compound having DPP-IV inhibiting activity, and the invention disclosed in claims 1-6 differs from this on the point that the substituent group at the 4-position of the bicyclo[2.2.2]octane ring is a pentyl group.

In addition, document 2 (page 32) discloses (S,S) 1-(2-amino-2-bicyclo[2.2.2]oct-1-yl-acetyl)-2,5-dihydro-1H-pyrrol-2-carbonitrile as a compound having DPP-IV inhibiting activity and having a bicyclo[2.2.2]octane ring in an N-(glycyl-substituted)-2-cyanopyrrolidine structure.

However, as disclosed in documents 3-8 (document 3, pages 48-62, 64-68, 70, 72-73, 87-103; document 4, page 35 J, K; document 5, page 18-20; document 6, pages 56, 77; document 7, page 29, Nos. 23, 28, page 30, Nos. 30, 32, 38; document 8, page 34, No. 39), a variety of compounds having amide groups at the 4- (or para-) position of cycloalkanes and heterocyclic rings are known as N-(cycloalkane-substituted-glycyl)-2-cyanopyrrolidines having DPP-IV inhibiting activity.

Therefore, conceiving of a compound having an amide group as the substituent group at the 4-position of the bicyclo[2.2.2]octane ring disclosed in document 1 could be easily achieved by a party skilled in the art.

In addition, documents 1-7 (document 1, page 15; document 2, page 59; document 3, page 10; document 4, page 17; document 5, pages 36-45; document 6, pages 39-47; document 7, pages 11-12) also disclose using an intermediate that protects these amino groups.

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/JP.2005/002389

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of: International Patent Classification (IPC)

Int. Cl<sup>7</sup> A61P3/10, 7/00, 7/10, 9/12, 13/08, 17/06, 19/02, 19/10, 25/28, 29/00,  
31/04, 31/18, 35/04, 37/96, 37/08, 43/00